REMARKS/ARGUMENTS

Claims 11, 13-18 and 26-33 are pending and under examination in the captioned application. The application has been amended. The specification has been amended. The claims have been amended. Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments. Applicants respectfully submit that the amendments are fairly based on the specification and respectfully request their entry.

Claim - Objections

The Examiner has objected to claims 11, 14, 26, 28 and 33 and suggested that the claims be amended to recite "Aequorea victoria" instead of "A. victoria". In response, Applicants have amended the claims to comply. Applicants request that the objections to the claims be withdrawn.

Specification - Objections

The Examiner has objected to two informalities in the specification. First, the Examiner again objected to the use of trademarks, specifically the improper use of TRIS® and suggested an acceptable term (TRIS® (hydroxymethyl) aminomethane hydrochloride) for Tris-HCl. Applicants have amended the specification to fulfill the requirement of the Examiner.

Secondly, the Examiner has objected to the specification because the sequence notation written as "SEQ ID No. 1" instead of "SEQ ID NO: 1". Applicants respectfully submit that the same objection was raised in an earlier Office Action dated October 24, 2003, and Applicants corrected these informalities in a response filed January 13, 2004.

Applicants respectfully submit that these amendments are fully supported by the specification and do not add new matter. Applicants request that the objections to the specification be withdrawn.

Claim Rejections - Enablement

The Examiner has again rejected the pending claims under 35 U.S.C. § 112, first paragraph, for lack of enablement. The sole issue remaining is whether or not the specification is enabling for any functional analogue of GFP. Applicants respectfully assert that the specification is enabling for GFP analogues containing the amino acid substitutions at the specified positions as claimed. Nonetheless, solely to expedite prosecution, Applicants have amended the pending claims by incorporating the Examiner's suggestion. Therefore, the rejection has been obviated. Applicants respectfully request that the rejection be withdrawn.

<u>Claim Rejections – Indefiniteness</u>

The Examiner has again rejected the pending claims under 35 U.S.C. § 112, second paragraph as being indefinite. The claims were rejected because (1) the Examiner

states that the term "functional analogue" is indefinite; and (2) the Examiner states that "the claim broadly recites that the modified GFP has a different excitation spectrum/ emission compared to the wildtype and there is no recitation of any improvements."

As stated above, Applicants respectfully submit that the claims have been amended, and the rejected term "functional analogue" has been removed. Therefore, the rejection has been obviated.

With regard to the property of GFP, while Applicants believe the claim language accurately describes the mutant GFP (e.g. different excitation spectrum and/or emission spectrum as compared to the wildtype GFP), the amendment is made to describe more specifically the changes as fluorescent intensity increases. Support of this can be found in Figure 5, and associated text (page 34, lines 16-18). Applicants believe that the rejection has been obviated.

Claim Rejections – Anticipation

The Examiner has rejected claims 11, 15-17 and 33, under 35 U.S.C. § 102(b), as being anticipated by Tsein et al. (U.S. 6,077,707) based on any functional analogue of GFP.

In response, Applicants respectfully submit that the amendments presented above have avoided the reference of "any functional analogue of GFP". In addition, Applicants submit that Tsein et al. does not teach a modified GFP comprising the following modifications: F64T, E222L and S175G. Applicants submit that the Examiner seems to

have misread the protein sequence listed on column 39 (SEQ ID NO: 4) of Tsein et al. Applicants submit that SEQ ID NO: 4 of Tsein et al. is that of an engineered fluorescent protein, utilizing preferred mammalian codons and optimal Kozak sequence (see column 2, lines 45-49). This sequence contains an additional Val(V2) between the first (Met) and second (Ser) amino acid sequence of the wildtype GFP sequence (SEQ ID NO: 2 of the instant application). Because of the addition of V2, the numbering of each of the subsequent amino acids of SEQ ID NO: 4 is shifted one from the wildtype sequence. As such, F64, E222 and S175 of the wildtype sequence appear as F65, E223 and S176 in SEQ ID NO: 4 of Tsein et al. None of the three amino acid sequences is changed from the wildtype sequence. Because Tsein et al. does not teach the triple modifications as claimed in claim 11, and because the language regarding functional analogues of GFP has been avoided, the rejection of claim 11 under 35 U.S.C. § 102(b) should be withdrawn.

As such, the rejection toward dependent claims 15-17 should also be withdrawn.

Applicants have amended claim 33. Claim 33 now depends upon independent claim 26, not claim 11. Applicants respectfully submit that an error was made in the amendment submitted on July 26, 2004. In that amendment, new claims 26-33 were introduced, separating the claim language for GFP with a sequence substitution at position S65 into the newly added claims. Claim 33 further defines amino acid sequence substitution at position 65. Unfortunately, a typographical error caused claim 33 to depend upon claim 11, while it was intended to depend from claim 26. Applicants

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respectfully request entering of this amendment and submit that the amended claim is in allowable form.

Applicants believe that the foregoing constitutes a full and complete response to all outstanding objections and rejections. Applicants further believe that this application is now in condition for allowance. However, should any issues remain, the Examiner is respectfully requested to telephone the undersigned at (732) 980-2875 for prompt resolution.

Early and favorable action is earnestly solicited.

Respectfully submitted,

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Tel: (732) 980-2875 Fax: (732) 457-8463 I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on <u>December 14, 2004</u>.

Signature:

Name:

Melissa Leck